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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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ROPES & GRAY  
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EXAMINER

KAUFMAN, C

ART UNIT	PAPER NUMBER
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1646

*28*

DATE MAILED:

07/20/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

**Advisory Action**

Application No.

09/021,660

Applicant(s)

BARON ET AL.

Examiner

Claire M. Kaufman

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1646

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 09 July 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 09 July 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See attached.

3. ☒ Applicant's reply has overcome the following rejection(s): See attached.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 57-81.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other:

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Continuation of 2. NOTE: The amendment if entered would raise many new issues requiring further consideration. The following are examples, but should not be considered as a comprehensive list of new issues: Proposed amended claim 57 and new claim 81 would raise new issues under 35 USC 112, first paragraph, due to the inclusion of "fragments thereof which bind to *patched*." This amendment would also raise issues under 112, second paragraph, because the structural relationship of the "fragments" (plural) is unclear. Applicants ask for cancellation of claims 76-81, but add claims 80 and 81 as new claims and have dependent claims. New claim 81 would raise new issues under 35 USC 112, first paragraph. New claim 86 would have no antecedent basis for "the undifferentiated mesodermal-derived cells".

The following claim interpretation is presented to aid Applicants in further prosecution of this or a CON or DIV of this case: In proposed claim 57 and subsequent proposed claims, the terms Indian hedgehog, Desert hedgehog, Sonic hedgehog are being interpreted as meaning these proteins consist of the amino acid sequence found in nature. That does not preclude these proteins from being recombinantly produced, but their amino acid sequence is the same as that found in the corresponding proteins isolated from an animal. This appears to agree with the use of the terms in the specification, where all references to, for example, Ihh, are to the protein with a sequence which is found in nature (*e.g.* p. 20, lines 21-17). The meaning of these terms appears to be distinct from that of a "hedgehog compound" as defined on page 11, lines 23-26, which includes analogs and derivatives of hedgehog proteins.

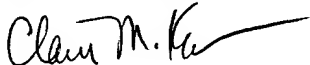
Continuation of 3. Applicants' reply would overcome the following rejection(s): the rejection under 35 USC 112, second paragraph, of claims 57 (with the exception relating to 'second compound comprising a TGF- $\beta$  compound), 61 and 62; and the rejection under 35 USC 102 with the above claim interpretation. Cancellation of claims 76-81 would moot all rejections of those claims (except as new redundantly numbered claims 80 and 81 would be rejected).

Continuation of 5. does NOT place the application in condition for allowance because: Arguments which were not previous addressed are addressed here. The rejection under 35 USC 112, second paragraph, would remain for 'second compound comprising a TGF- $\beta$  compound,'

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since Applicants maintain that TGF- $\beta$  need not be the active ingredient. The Examiner maintains that it is critical for the skilled artisan to know whether or not TGF- $\beta$  affects the method. If it does or does not will determine how much should be present and what if anything it should be present in combination with, so the metes and bounds (boundries) of the claimed subject matter are unclear. Applicants do not have written description for the claimed methods. Reduction to practice is not always required, however a sufficiency of information in the specification is necessary to allow the skilled artisan to recognize the Inventor could envisage (practice) the claimed methods with a representative number of embodiments sufficient to support the class(es) of compounds used. There are facets of the methods for which this is not the case, e.g., hh derivatives. Also, binding patched is not equivalent to activating patched, and depending on the intended meaning of fragments ... which bind to patched, the proposed claims might not have sufficient written description. Reduction to practice is not an automatic requirement to meet written description, but one must be able to envision the class of compounds--not every single compound within the class but a representative number, and it is maintained that the skilled artisan cannot do this in this case. As to clarification about cross-species activation of ptc by hh, as addressed in the previous Advisory action: While mouse Shh might have some function in Drosophila, what function if any Drosophila hh would have in a much more complex organism, such as a mouse, is unpredictable. Further, as shown by Applicants' exhibit A (Chang et al., 1994), there are clearly specific instances in which a vertebrate hh can function in Drosophila, but one would not reasonably expect the reverse to be true. The abstracts of Exhibit B show that a hh protein having an amino acid sequence found in nature can function to induce to formation of hematopoietic cells in embryonic vertebrate cells. These findings do not contradict the holding of lack of enablement.

Claire M. Kaufman



Patent Examiner, AU 1646

July 19, 2001